REMARKS

Applicants wish to thank Examiner Shin-Lin Chen for interviewing with Applicants' representative on October 18, 2007. Applicants respectfully request entry of amendments to claims 20-22 and 24, and cancellation of claim 23. Claims 1-19 and 26-28 are withdrawn, without prejudice or disclaimer. Support for the amendments can be found throughout the specification, including p. 3, ll. 13-28; p. 7, l. 16 bridging to p. 8, l. 2, p. 14, ll. 1-15; p. 17, ll. 24-26, Examples 4, 6, 8, and 10-12, and the originally filed claims and, therefore, do not add new matter.

Applicants submit that pending claims 20-22, 24, 25, and 29 are in condition for allowance, and respectfully request that the claims as amended be entered.

Rejections Under 35 U.S.C. §112, First Paragraph

Claims 20-22, 24, 25, and 29 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking written description.

Applicants traverse the rejection as it might apply to the amended claims, including claims dependent therefrom, for the reasons given below.

The Office Action alleges, in pertinent part, that the specification does not disclose a hollow fiber formed from a material which has a pore size of about 0.1 μm to 0.3 μm, however, membranes having such a pore size are expressly disclosed. While not acquiescing to the reasoning offered in the Action, in order to expedite prosecution toward allowance, the claims have been amended to recite "membrane" instead of "material." As such, one of skill in the art could envision the hollow fiber of the claimed invention, and would appreciate that the inventors were in possession of the genus as claimed at the time the invention was filed.

For these reasons, Applicants respectfully request that the rejection be withdrawn.

Claims 20-22, 24, 25, and 29 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement.

Applicants traverse the rejection as it might apply to the amended claims, including claims dependent therefrom, for the reasons given below.

The Office Action alleges, in pertinent part, that "while being enabling for an extracorporeal bio-artificial liver device comprising an apparatus containing cells of the cell line deposited as ATCC accession No. CRL-12461 cultured in serum free medium on a surface of the device for expressing albubinalpha[sic]-1-antitrypsin, factor V, complement C3 and antithrombin III etc., wherein the surface is contained within a hollow fiber cartridge, does not reasonably provide enablement of the extracorporeal bio-artificial device set forth above, wherein the device provides liver specific biological activity at a level sufficient to sustain a subject a subject having a liver disorder or compromised liver function, a method of using the cells to provide bio-artificial liver support for the subject, and a method of treating a subject having compromised liver function, such as Fulminant hepatic failure (FHF)."

Notwithstanding the amendments, the Action states that "[c]laims 20-25 encompass using any cell line, derived from parent C3A cell line," however, the claims had been amended previously to recite an apparatus "containing cells of the cell line deposited as ATCC accession No. CRL-12461." Thus, it is not clear as to how the Action has come to this conclusion, and Applicants respectfully submit that the scope as interpreted in the Action is incorrect.

Nevertheless, claim 20 has been amended to recite that "the cells are cultured in serum-free medium on a surface in the device and express one or more proteins selected from the group consisting of albumin, alpha-1-antitrypsin, factor V, complement C3, antithrombin III, and transferrin," which is expressly stated in the Action to be enabled. As such, the rejection as applied to claim 20 is rendered moot.

For the method claims, the instant specification acknowledges the problem to be solved; i.e., use of hepatocytes (cell lines) that produce liver bio-products without concomitantly introducing cryptic infectious agents that are normally associated with serum (see, e.g., p. 3, ll. 13-28). In other words, the problem to be solved is in producing and using hepatocyte cell lines adapted for normal growth and maintenance in serum free media. The specification expressly provides for such cells, and such cells have been deposited as ATCC accession No. CRL-12461. Further, one of the properties of these cells is that they produce one or more specific secreted proteins (Example 4 and Figure 1). Moreover, these cells exhibit normal (and predictable) growth profiles (Example 6). Thus, the specification is clear in that one way to eliminate

concomitant introduction of cryptic agents into blood using hepatocytes cell lines is to produce cell lines that do not require growth in serum, and the specification provides for the making and using of such cells therein (Example 1). Accordingly, in view of one of the admittedly enabled uses of such a cell line in the production of "an extracorporeal bio-artificial liver device comprising an apparatus containing cells of the cell line deposited as ATCC accession No. CRL-12461 cultured in serum-free medium on a surface of the device for expressing albubinalpha[sic]-1-antitrypsin . . . wherein the surface is contained within a hollow fiber" (p. 3, Item 4, first paragraph), claim 20, as amended, recites such a device.

Applicants submit that given the demonstrated properties of the cells as claimed, especially with respect to 1) the ability of these cell to grow in serum free media and 2) the observed secretion of proteins from these cells, it is clear that a device as claimed would release proteins from the cells contained therein to blood perfused through the device, as secretion of such proteins is an inherent property of the cells contained therein (i.e., products of identical chemical composition can not have mutually exclusive properties; see, e.g., In re Spada, 15 U.S.P.Q.2d 1655 (Fed Cir. 1990)). Further, since hollow fiber devices comprising cells were well known in the art to allow for blood perfusion, which cells secrete materials into the perfusate (see, e.g., U.S. Pat. Nos. 4,675, 002, 4,853,324; GB Pat. No. 2,221,857A; Knazek, Fed Proc (1974) 33:1978-1981; Ku et al., Biotechnol Bioeng (1983) 23:79-95; Tharakan et al. Biotechnol Bioeng (1986) 28:1605-1611), and since such hollow fiber devices were commercially available for the purpose of culturing cells for perfusion at the time the present invention was filed (see, e.g., p. 20, ll. 9-25 of the present specification), it cannot be argued that one of skill in the art would not find such use of cells routine or that the skilled artisan would not expect cells grown in such devices to retain their ability to secrete proteins.

Applicants submit that since it is well known that subjects suffering from FHF have low albumin (see, e.g., http//homepage.mac.com/guitarbloke/Surgical_sieve/Hepatobiliary/Liver/Hepat_FHF.html), a specific protein that is produced by the cells as claimed (see, e.g., Example 4, Table 1), one of skill in the art would expect that a device which increases albumin in the blood would be effective in FHF. Again, the position taken in the Action regarding clinical efficacy is not within the purview of the United States Patent and Trademark Office. As stated in Scott v. Fenny, 32

U.S.PQ.2d 1115, 1120 (Fed. Cir. 1994), "[t]esting for the full safety and effectiveness of a prosthetic device is more properly left to the Food and Drug Administration (FDA)." Also, with respect to Strain et al., the statements attributable to the reference are inapplicable to the instant invention because the cells as claimed are not primary hepatocytes, and are in fact phenotypically stable (see Examples 4 and 6). Accordingly, any conclusions drawn based on properties of primary hepatocytes in view of the defects outlined in Strain et al. are inapposite. Further, with respect to the statement that "it has been assumed, but not yet proven, that simple 'flow through' BAL systems achieve this[optimal ex vivo maintenance of hepatocytes]," such a broad statement is inaccurate given the results provided in the Declaration of record, which demonstrate (clinically) the general premise that the use of hepatocyte cell lines (not primary hepatocytes) in a bio-artificial liver is effective for the scope of the invention as claimed. Thus, Applicants respectfully submit, that the amended claims are enabled for a device that provides serum-contaminant free liver bio-products, particularly albumin, to a subject using an extracorporeal bio-artificial liver device as presently claimed.

Therefore, one of skill in the art could practice the invention as claimed, in the absence of undue experimentation, because 1) as the specification provides prediction of function based on tested and workable materials and designs of prosthetics that were well known in the art at the time the application was filed, the skilled artisan would know how to make the device, and 2) based on evidence of record, as the device as claimed would be expected to possess the property of providing hepatocyte cell line-derived proteins free of serum contaminants, the skilled artisan would know how to use the device. That is all that is required.

For these reasons, Applicants respectfully request that the rejection, including as it may be applied to the amended claims, be withdrawn.

Conclusion

Applicants submit that pending claims 20-22, 24, 25, and 29 are in condition for allowance, or are in better condition for appeal. The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this submission.

Please charge $525.00 to Deposit Account No. 07-1896 to cover a Three Month Extension of Time fee. The Commissioner is hereby authorized to charge any additional fees required by this submission, or credit any overpayments, to Deposit Account No. 07-1896 referencing the above-identified docket number.

Respectfully submitted,

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Daryl A. Basham, J.D., Ph.D.
Registration No. 45,869
Telephone: (858) 677-1429
Facsimile: (858) 677-1465

DLA Piper US LLP
4365 Executive Drive, Suite 1100
San Diego, California 92121-2133
USPTO Customer Number 28213